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14. ABSTRACT
The Integrative Cardiac Health Project (ICHP) aims to lead the way in Cardiovascular Disease (CVD) Prevention by conducting novel research utilizing a Systems Biology / personalized medicine design to discover and develop practical, effective and preemptive integrative approaches in order to detect and combat CVD earlier before it affects the quality of life. ICHP's ultimate goal is to translate our evidenced-based research findings for application into clinical practice. A translational research approach will provide the ability to find novel disease markers, optimal prevention and holistic treatment approaches, and a unique venue for future research as the "virtual laboratory" for optimal comprehensive health prevention in the military beneficiary population. This research method also allow us to further hypothesize and define relationships between CVD, other cardio metabolic disease states and maladaptive behavior patterns unique to service members such as pre-diabetes, stress, overweight and sleep disorders with the aim of targeting these disorders in a pre-clinical phase. Using an integrative, interdisciplinary preventive health approach, ICHP has shown that an individual's cluster of CV risk factors can be effectively targeted and improved.

15. SUBJECT TERMS
Lifestyle; Cardiovascular Disease (CVD); Prevention; Behavior Modification; Genomics; Metabolic Syndrome; PreDiabetes; Diabetes; Obesity; Stress; Sleep; CVD Risk Reduction

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

   Cardiovascular disease (CVD) is the most common and costly preventable health problem. Cardiovascular health requires identification of reversible factors to guide risk reducing lifestyle management interventions. However, CVD risk assessment tools lack precision, delaying diagnosis and preventive therapies. There is an urgent need for more accurate CVD risk assessment and risk reduction tools, especially in the military where CVD risk is magnified by multiple deployments, major trauma, sleep deprivation, post-traumatic stress, and depression. The main objectives of this research are to: 1) Improve accuracy of early CVD risk assessment focusing on military-relevant factors, and; 2) Develop/test military-specific behavioral interventions for CVD risk reduction in domains of diet, exercise, stress and sleep. ICHP aims to support research focused on preclinical CVD risk assessment/reduction in military populations and personalized strategies for CVD lifestyle management intervention. Scope of the research includes the following study designs: 1) a prospective registry; 2) a comparative cohort study: CVD risk in Wounded Warriors vs healthy service members; 3) a randomized controlled trial evaluating the efficacy of Cognitive Behavioral Therapy in insomnia patients, and; 4) an observational cohort design by gender comparing personalized behavioral intervention with usual care; Comparative cohort study to define prevalence of increased CVD risk in young military beneficiaries using clinical, psychosocial, behavioral, and biochemical measures. ICHP, a DOD Center of Excellence, supports the MHS Strategic Focus on Health, targeting precision CVD risk assessment and reduction for military service members to improve health outcomes and reduce cost.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

   Cardiovascular Disease (CVD); Prevention; Lifestyle; Behavior Modification; Genomics; Metabolic Syndrome; PreDiabetes; Diabetes; Obesity; Stress; Sleep; CVD Risk Reduction

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

   What were the major goals of the project?

   Study 1: Cardiovascular Health Program (CHP) Registry, a lifestyle management intervention (LMI) specifically designed for the military population (continuing effort):

   1) To evaluate and enhance the benefits of patient-centric tools for comprehensive CVD risk assessment and reduction in the context of longitudinal outcomes.
   2) To evaluate and enhance the ICHP CHP LMIs to improve patient-centric CVD risk reduction in the context of longitudinal outcomes.
   3) To analyze self-management behaviors (nutrition, exercise, stress and sleep) that make the military population more vulnerable to CVD due to hazardous occupational exposure.
   4) To improve measures of endothelial function and/or surrogate measures of atherosclerosis utilizing the ICHP CHP lifestyle management intervention in subpopulations (i.e. Caucasians vs. Non Caucasians).

5) To capture patient generated data, including data (motivation, joys, barriers and self-efficacy) not routinely captured in MTF electronic health records to facilitate patient and family engagement to optimize outcomes.

Study Milestone	Timeline (Months)	% Completed
Met enrollment prediction of 35 new patients per quarter (% = # actual prospectively enrolled /cumulative quarterly projected enrollment during award period of performance)	4-36	13%
Patients maintain active participation in the ICHP CHP Registry after enrollment (% = # active patients/# total prospectively enrolled during award period of performance)	1-36	83%
100% pre-clinical states identified at ICHP appointments reported to patient's PCP for tracking and follow-up	12-36	100%
Administrative and Clinical ICHP portals in RIMS connected with interfacing capability	6-12	60%
Quality Assurance process in place for trans clinical team review and chart documentation	12-36	100%
ICHP translational research successfully incorporated family history into prediction tools and identified patients at" high risk" for heart attack and stroke who were otherwise told they were" low risk"	12-36	100%
100% dissemination of comprehensive CV health report to providers at baseline, 6 months and 1 year	1-60	100%
Distribute Healthy Living Toolkits to CHP participants	Annually	100%
Deliver 1 new Healthy Living Cookbook	24	40%
Develop 1 new clinical decision support tool for providers	36	75%
Deliver 1 new portable stress management (Tension Tamer) tool	24-36	50%
Develop ICHP Healthy Lifestyle Index	24-36	100%
Comparative analyses of CHP LMI outcomes performed	Annually	90%
Findings disseminated to sponsor, staff, data safety monitor, SAB and scientific communities through required reports, abstract, manuscript submissions	Annually	100%
Cardiovascular Ultrasound Technologist trained	8	0%
Protocol amendment approved	6	0%
Collection of endothelial function measures initiated	8	0%
Interim analysis of data to show impact of endothelial function measures on CHP LMI	Annually	0%
Development and completion of data dictionary	12-24	80%
All ICHP patient generated data migrated to RIMS	6-12	75%
Completed RIMS structured team appointments in domains of nutrition, exercise, stress and sleep	12-36	40%
All data reviewed and quality checks completed	Quarterly	100%
Interim data analysis performed	Annually	100%
New phenotype of CVD risk profile identified	24-36	20%
Manuscript published	24-36	40%

Study 2: Assessing Risk Factors for Cardiovascular Disease in Individuals with Major Injury (With or Without Amputation) versus No Injury (continuing effort):

1) To identify the specific risk factors that may contribute to an increased CVD risk in military personnel with major injury.
2) To develop a comprehensive CVD risk profile in military personnel with major injury.
3) To theorize the pathophysiology behind the changes in CV risk profiles in those individuals with major injury.
4) To develop treatment strategies specifically targeted for a more precise CV risk

stratification in populations with major injuries.

Study Milestone	Timeline (Months)	% Completed
All ICHP supported data collection completed as coordinated with PI.	12-36	100%
All appropriate surveys scores and ICHP CV risk score calculations completed, validated and recorded in research record.	1-36	25%
Support and consult for data analysis	1-36	0%

Study 3: CHP Cognitive-Behavior Therapy for Insomnia (CHP CBT-I) Study (continuing effort):

1) To evaluate the feasibility and acceptability of CBT-I within the CHP program (Phase 1; N=12).
2) To determine the variability of the effect of CHP compared to CHP + CBT-I on the primary outcome (sleep efficiency) (Phase 1).
3) To determine the effectiveness of CHP compared to CHP + CBT-I on the improvement of sleep outcomes in a subset of CHP patients diagnosed with insomnia (Phase 2; N-64).
4) To determine the effectiveness of CHP compared to CHP + CBT-I on symptoms of fatigue, insomnia severity, depression, perceived stress, and sleep-related quality of life (Phase 2).
5) To examine data regarding the impact of the CHP program compared to CHP + CBT-I on secondary cardiovascular risk factors in a subset of CHP patients with insomnia (Phase 2).

Study Milestone	Timeline (Months)	% Completed
1st participant consented, screened and enrolled	1	100%
CBT-I intervention begins	2-3	100%
Phase 1 data analyzed for CBT-I feasibility	7-8	0%
Report findings from 6 month follow-up assessments through abstracts/presentations to sponsor, research team, data safety monitor, SAB and scientific community.	8-9	0%
Modifications complete and processes finalized	9	0%
1st participant consented, screened and enrolled in Phase 2, Study 3	9	0%
Phase 2, Study 3 begins	9	0%
Report findings from overall studies to sponsor, research team, data safety monitor, SAB, and scientific community.	Quarterly	100%
Manuscript submitted for publication	35-36	0%

Study 4: UPLIFT (Ultra-Personalized Laboratory-Risk Intervention For Treatment) for Cardiovascular Health: Cardiovascular (CV) Disease (CVD) Risk Study (new effort):

Study 4 UPLIFT Part 1a/b Specific Aims 1a1, 1a2:

Part 1 Specific Aim 1a1: In a retrospective observational cohort design, determine the prevalence of moderate and high risk CVD stratification (using novel predictive biomarkers) in a healthy pre-deployment established cohort traditionally considered at low risk for CVD with stratification by sex. **Part 1 Specific Aim 1a2:** In relation to the pre-deployment defined CVD moderate/high versus low CVD risk, to characterize the incidence (over time and by sex) of CVD related new diagnosis and/or major morbidity/mortality using MHS databases of inpatient/outpatient diagnoses (new, 1st time) between 2004-2015 providing potentially up to 10 years of follow-up data.

Study Milestone	Timeline (Months)	Completed
Signed CRADA with ABBOTT Labs.(& CRADA Development)	6-12	70%
Signed CRADA with Labcorp (Liposcience).(& CRADA Development)	6-12	70%
Letter of support received from Army Analytic Unit.	6-12	50%
Local IRB submission/approval at WRNMMC, Fort Belvoir	6-12	20%
All approvals for protocol implementation	8-12	0%
Local IRB approval at WRNMMC received.	8-12	0%
All approvals received for protocol implementation.	8-12	0%
All sample shipment for testing completed to ABBOTT	12-24	0%
All sample shipment for testing completed to Liposcience	12-24	0%
Testing results received from ABBOTT Labs & verified	18-24	0%
Testing results received from Liposcience & verified	18-24	0%
All result data reviewed and cleaned in preparation of analyses	18-24	0%
Data exploration, display and final coordination of analysis plan completed	18-24	0%
All sample testing data cleaned and QC for final datasets for analysis	18-28	0%
1st Manuscript completed and submitted	24-30	0%
Manuscript accepted, second manuscript preparation	32-36	0%
New CVD diagnosis (inpatient/outpatient) surveillance plan completed and submitted to MHS database manager collaborators (e.g. Army Analytic Unit or other to be determined)	18-24	0%
Redacted data set including CVD risk assessment parameters, demographics, clinical and laboratory data linked to MHS database surveillance outcomes returned for final analysis	21-30	0%
2nd round of surveillance data for CVD relevant diagnoses & events completed with consideration for a second manuscript	36-60	0%

UPLIFT STUDY 4 Part 2 Specific Aims 2a, 2b (primary), 2c/2d (secondary):

Specific Aim 2a: Determine the prevalence of hsTnI (coupled with us-CRP, suPAR, NT-pro-BNP and Gal-3) risk predictive elevations [sex adjusted levels published as surrogate markers of CVD mortality and major events] in patients with and without evidence of obstructive CVD by CIS.

Specific Aim 2b: Discovery of novel patterns of validated biomolecular CVD risk markers (distinct from traditional CVD risk calculators] and systemic inflammation, by sex, for further research in the context of genetic profiling and potential differences in responses to therapeutic lifestyle management and preventive therapeutic interventions.

Specific Aim 2c: To determine, by sex, validity of using a screening questionnaire built on a single-question for each of the major CVD risk confounders in relation to more comprehensive validated questionnaires.

Specific Aim 2d: Characterize novel patterns of systemic inflammation contributing to atherosclerosis progression, by sex, that may increase rates of major CVD events in the context of long-term surveillance within the MHS diagnostic databases.

Study Milestone	Timeline (Months)	% Completed
1st participant consented, screened and enrolled	12-18	0%
First blood draw processed, QC'd for labeling, rapid separation, prepare aliquots, rapid freezing to preserve troponin stability	12-18	0%
Study 2 begins	12-18	0%
30% of enrollment goals achieved	4-18	0%

40-50% enrollment goals achieved	24-36	0%
over 70% enrollment goals achieved	37-60	0%
25% of subjects completed 1 year follow-up (of total with N~150-200)	28-36	0%
40-50% of subjects completed 1 year follow-up (of total with N=~240-300)	37-59	0%
Interim analysis plan finalized with statisticians	24-28	0%
Interim analysis for pilot data presentation completed	32-36	0%
Iterative analyses with final comprehensive data review completed for presentation and manuscript preparation	37-60	0%
Development and completion of data dictionary	12	75%
30% of sample shipment for testing to ABBOTT completed	24-32	0%
50% All samples shipped for testing to Liposcience	33-48	0%
Testing results received from ABBOTT Labs & verified – 30% complete by 36 months	24-60	0%
Testing results received from Liposcience & verified – 30% complete by 36 months	24-60	0%
>70% of subjects enrolled with results	48-60	0%
Data Safety Monitor presentation content completed	24-36	0%
Completed Data Safety Monitor review with implementation of recommendations in progress for completion	28-36	0%
Continued Data Safety Monitor data review for option years and ongoing enrollment	24, 48	0%
Sample testing data cleaned and QC for final spreadsheet	48-56	0%
1st Manuscript completed and submitted	36-42	0%
Second manuscript preparation draft	36-58	0%
Dissemination of initial findings (abstracts, presentation, publication, DOD reports) with summary of implications for MHS health promotion priorities	36-60	0%
Obtain outcomes surveillance data set on 30-40% of total enrollment cohort	37-48	0%
Obtain outcomes surveillance data set on 50-60% of total enrollment cohort	52-60	0%
Summary interim data report, presentation and manuscript preparation	52-60	0%
Dissemination of initial findings (abstracts, presentation, publication, DOD reports) with summary of implications for MHS health promotion priorities	52-60	0%

Specific Aim (Relevant to Part 1 and 2): Establish a biologic sample repository (plasma, serum, whole blood, saliva, DNA, RNA) for staged testing and cost-effective approaches for evolving hypotheses testing and biomarker modeling/validation.

Study Milestone	Timeline (Months)	% Completed
1st 30% of samples collected, processed and recorded in tracking	28-39	0%
All study samples collected, processed and recorded in tracking system	37-60	0%

Specific Aim: To determine the annual incidence of new CVD relevant diagnoses (hospitalizations, outpatient visits) in study cohorts (from Part 1a, 1b, 2 and 3) following primary enrollment and compare this incident rate to matched healthy controls from the MHS diagnostic coding data repository.

Study Milestone	Timeline (Months)	% Completed
Implementation of outcomes surveillance plan and data obtained for final analysis and manuscript preparation Part 1a	25-32	0%
Implementation of outcomes surveillance plan and data obtained for final analysis and manuscript preparation (Part 1b)	52-60	0%
Implementation of outcomes surveillance plan and data obtained for final analysis and manuscript preparation (Part 2)	48-60	0%

Specific Aim: To facilitate research study enrollment and data-capture on site (WRNMMC Cardiac Cath Lab, Immunization Clinic, Internal Medicine Prevention & Health Clinic, FBCH Cardiology, etc.) as well as institutional biorepository inventory tracking and required monitoring of individual sample locations/movements/disposal.

Study Milestone	Timeline (Months)	% Completed
Database structure verified to accommodate mission requirements and improve workflow efficiency	18-48	30%
ICHP study data migrated to RIMS	18-60	0%
Process for sample bar coding and database tracking established and verified	18-24	0%
Biorepository database tracking system established in support of protocol	24-36	10%

What was accomplished under these goals?

Study 1: Cardiovascular Health Program (CHP) Registry

The following major activities have been accomplished in the past year:

1) Reviewed by Scientific Advisory Board and approved
2) 18 participants consented for registry; prospective enrollment=206
3) 328 participants on-site visits (18 new participants, 310 follow-on program visits)
4) 444 coaching calls (off-site program) made by clinical team experts
5) Streamlined outcome assessment with 100% quality control process in developed and implemented. Process working well to reduce backlog; 28 successful Outcome 1 program completers.
6) Input of baseline data in RIMS for those participants who did not have metric data entered when starting program; 100% quality control process put in place
7) Enhancement of prediabetes track to improve our conversion from prediabetes to normal glucose levels
8) Development of strategies within our four pillar program to target lowering insulin levels for CVD prevention and also cancer and brain health benefit
9) Work begun to establish a "setting the stage" initiative for pre-emptive behaviors in the military setting
10) Continuing to develop patient tools, such as military-specific cookbooks to accommodate the busy and high stress environment
11) Preparation begun to modify ICHP's Research Information Management System to accept and analyze personalized behavioral approaches for health behavior change
12) Development &/or updating of program marketing materials to reflect current mission/ vision (i.e. ICHP program brochure, onsite ICHP model display boards, patient handout materials)
13) Data analysis of clinical outcomes on Active Duty and Retired Senior Leaders who have participated in CHP in preparation for MHS Conference abstract submission and manuscript publication
14) Analysis continues of our biometric data to outline differences between men and women and between ethnicities for CVD
15) ICHP reviewed manuscript per editor invitation as subject matter expert in family history as CVD risk factor for European Journal of Clinical Investigation

16) Exploring possible collaboration with Tod Downen, VP of Health Research Tx (part of Health Outcomes Center of Excellence that works with the Navy, based in Portsmouth) using Military Healthcare Data Repository (MOU and SOW already in place)
17) Outcomes manuscript in development; continued tallying of medications in patient populations
18) New developed advanced cardiovascular disease training program for new ICHP Nurse Practitioners
19) Development of new referral tracking system to improve participant outcomes
20) Annual Continuing Review submitted to WRNMMC IRB via eIRB system on 27 Jan 17; approved 27 Mar 17; acknowledged by MRMC HRPO pending.

Major Findings:

Below find abstracts of our results published within the past year:

1. Kashani M, Eliasson AH, Walizer EM, Fuller CE, Engler RJ, Villines TC, Vernalis MN. Early empowerment strategies boost self-efficacy to improve cardiovascular health behaviors. *Glob J Health Sci* 2016 Feb 2;8(9):55119. doi: 10.5539/ghis.v8n9p322.

Background: Self-efficacy, defined as confidence in the ability to carry out behavior to achieve a desired goal, is considered to be a prerequisite for behavior change. Self-efficacy correlates with cardiovascular health although optimal timing to incorporate self-efficacy strategies is not well established. We sought to study the effect of an empowerment approach implemented in the introductory phase of a multicomponent lifestyle intervention on cardiovascular health outcomes. **Design:** Prospective intervention cohort study. Methods: Patients in the Integrative Cardiac Health Project Registry, a prospective lifestyle change program for the prevention of cardiovascular disease were analyzed for behavioral changes by survey, at baseline and one year, in the domains of nutrition, exercise, stress management and sleep. Self-efficacy questionnaires were administered at baseline and after the empowerment intervention, at 8 weeks. **Results:** Of 119 consecutive registry completers, 60 comprised a high self-efficacy group (scoring at or above the median of 36 points) and 59 the low self-efficacy group (scoring below median). Self-efficacy scores increased irrespective of baseline self-efficacy but the largest gains in self-efficacy occurred in patients who ranked in the lower half for self-efficacy at baseline. This lower self-efficacy group demonstrated behavioral gains that erased differences between the high and low self-efficacy groups. **Conclusions:** A boost to self-efficacy early in a lifestyle intervention program produces significant improvements in behavioral outcomes. Employing empowerment in an early phase may be a critical strategy to improve self-efficacy and lower risk in individuals vulnerable to cardiovascular disease.

2. Eliasson A, Kashani M, Fuller C, Walizer E, Engler R, Villines T, Vernalis M. Targeted behavioral interventions improve disturbed sleep. *Sleep* 2016;39:A397.

Introduction: Sleep is an established risk factor for cardiovascular disease (CVD). CVD prevention programs are an ideal setting to assess patients for disturbed sleep. For our CVD prevention program, we report the frequency of disturbed sleep and improvement of important outcomes. **Methods:** At baseline, patients completed validated questionnaires: Berlin Questionnaire for sleep apnea, Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale

(ESS), and Stanford Fatigue Scale. After CVD risk assessment by a nurse practitioner, patients attended a healthy lifestyle workshop with didactics on healthy sleep practices, experiential stress reduction, and food demonstration. All patients received personalized lifestyle prescriptions. Patients with abnormal sleep surveys received customized sleep recommendations. Over 12 months, patients were coached on diet, exercise, and stress management. Validated surveys were repeated at graduation. Means and standard deviations provide descriptive statistics. Two sample t-tests measure statistical significance for changes from baseline to graduation. **Results:** Of 455 consecutive program completers, 59% women, there were 61% white, 31% black, 4% Hispanic, 2% Asian, 2% other. Fiftyone patients (11%) entered the program with previously diagnosed sleep apnea. Screening for sleep apnea was positive in 217 more patients (48%) consequently referred for polysomnography. Of the remaining 187 patients (41%), 68% had poor sleep quality (mean PSQI 7.8±2.8, normal sleeper <5 points), mean sleep duration 6.6±1.2 hours, ESS 7.3±4.4, and fatigue score 3.4±2.2. Of patients with poor sleep quality (68%), PSQI improved 2.2 points, $p<0.001$; 54% improved sleep duration 30 minutes, $p=0.007$; 71% improved ESS 3 points, $p<0.001$, and 58% improved fatigue 1.2 points, $p<0.001$. **Conclusions:** Our CVD prevention program provides an opportune mechanism to identify sleep disturbances. Nearly 2/3 of our population screens positive for sleep apnea and a majority of the remainder experience poor sleep quality and duration. Targeted interventions for improved sleep are effective and support CVD risk modification.

3. Engler R, Kashani M, Eliasson A, Walizer E, Fuller C, Villines T, Vernalis M. Blood pressure elevations below hypertension threshold linked to insulin resistance and dyslipidemia: An under-recognized cardiovascular disease risk phenotype. Presented at Military Health System Research (MHSRS) Symposium 2016.

Background: Cardiovascular disease (CVD) morbidity/mortality risk has been directly correlated to blood pressure (BP) levels with lower levels, even below “normal ranges”, associated with reduced CVD risk. Yet current clinical guidelines only address treatment for frank hypertension (equal/over 140/90 mmHg).There is increasing interest in earlier and more precise identification of CVD risk particularly for enhanced lifestyle management interventions to prevent disease and reduce lifetime risks. Metabolic dysfunction characterized by insulin resistance predicts future risk for type 2 diabetes mellitus (T2DM) and is potentially reversible. The homeostatic model assessment (HOMA) is a calculated value that reflects hepatic insulin resistance (IR). Early preclinical diabetes with increased IR affects a large population (86 million Americans) and has gone largely unrecognized. Improving the precision of CVD risk assessments in order to guide earlier more effective intervention strategies can reduce the burden of future CVD risk complications. **Methods:** Between July 2005 and July 2015, consecutive subjects entering the Integrative Cardiac Health Project (ICHP) Registry (a 12-month prospective CVD Risk Reduction Program) were assessed for BP category and prevalence of metabolic risk factors by measuring anthropometrics and CVD-relevant laboratory parameters including insulin resistance by HOMA. HOMA values greater than 2.0 to 3.0 are associated with increased CVD risk in adult populations. BP was categorized as not elevated (less than 120/80), modestly elevated (between 120/80 and 140/90, also described as prehypertension) and hypertensive (equal/over 140/90). Comparisons were made between subjects with no BP elevation, modest BP elevation and hypertensives for differences in CVD risk factors using t-test analysis. These BP groups were compared for the following CVD risk parameters: fasting glucose (Gluc), hemoglobin A1C (HgbA1C), HOMA-IR, low density lipoprotein (LDL), high

density lipoprotein (HDL), triglycerides (TG), body mass index (BMI), and waist circumference (WC). **Results**: Of 352 subjects (56% women, mean age 53 ± 13.5years, 61% white, 22% black, 5% Hispanic), 114 (32%) had no elevation in BP,154 (44%) had modest elevation in BP and 84 (24%) were hypertensive. There were no differences between the hypertensive group and those with modest elevation in BP. There were significant differences in means (+/- SD: standard deviation) between those without elevated BP and the group with modestly elevated BP for the variables detailed: Gluc [93.9(16.7) vs 100.6(14.9), p=0.001]; HgbA1C [5.5(0.06) vs 5.7(0.06), p=0.02]; HOMA [2.89(2.6) vs 3.75(3.8), p=0.01]; HDL[60.4(17.0) vs 55.2(13.6), p=0.009]; TG [97.6(50.7) vs 115.7(66.1), p=0.012]; BMI[28.2(5.8) vs 30.5(5.5), p=0.0006]; WC [94.3(15.1) vs 102.8(14.1), p=0.0001]. There were no significant differences in LDL levels [108.5(28.7) vs 115.0(38.0), p=0.12]. **Conclusion**: We demonstrate that among subjects with pre-hypertension, there is a significant prevalence of insulin resistance, dyslipidemia and obesity. Modest elevations in BP may identify subjects with metabolic syndrome who may benefit from enhanced preventive interventions. Given the many military service associated confounders exacerbate CVD risk, there is a need for improved earlier diagnosis of clinical conditions that can and should be addressed to maintain optimum health of the force.

4. Kashani M, Eliasson A, Walizer E, Fuller C, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Multidisciplinary cardiovascular team review captures preclinical disease. *J Am Coll Cardiol*. 2017; 69(11S):2103. doi.org/10.1016/S0735-1097(17)35492-X

Background: To ensure uniform application of AHA/ACC assessment guidelines for our 12-month cardiovascular (CV) health program and for early identification of preclinical disease, we conduct a CV team review of each patient with input from each team expert: nurse practitioner (NP), dietitian, exercise physiologist, stress coach, cardiologist and sleep specialist.

Case: Patients complete validated lifestyle questionnaires, anthropometrics and lab tests upon entry. The following 4 asymptomatic women with no heart disease were initially classified low risk by Framingham risk score (FRS).

Age	Sex	Race	FRS	Premature Family History	Body Mass Index (kg/m^2)	Blood Pressure (mmHg)	Glucose (mg/dL)	Exercise (min/wk)	Stress Score	New Sleep Apnea	# New Risks Captured
30	F	White	Low	***Pos***	***33.8***	101/65	95	***100***	***High***	***Pos***	5
49	F	White	Low	***Pos***	***31.7***	113/80	98	**30**	Low	***Pos***	4
65	F	White	Low	***Pos***	***37.0***	***148/80***	***108***	**105**	Low	Neg	5
46	F	Black	Low	***Pos***	***31.2***	***122/85***	96	225	***High***	***Pos***	5

Decision-making: The NP leads a review, a mechanism to assign CV risk thresholds to guide intensity of interventions. The 4 patients were reclassified as high risk per positive family history. Based on reclassification, the team identified new risk factors/preclinical disease: obesity, hypertension/prehypertension, prediabetes, sedentary lifestyle, high stress and sleep apnea prompting intensive recommendations for lifestyle modification. **Conclusion:** These cases highlight the value of a methodical, integrative and systematic CV team review as a venue to enhance identification of risk factors in the preclinical state in order to improve precision of interventions, enhance safety and empower patients.

5. Kashani M, Eliasson A, Fuller C, Walizer E, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Arresting insulin resistance with an integrative health intervention. *J Am Coll Cardiol*. 2017; 69(11S):1853. doi.org/10.1016/S0735-1097(17)35242-7

Background: Insulin resistance (IR) is the first signal of glucose dysmetabolism. IR precedes the development of prediabetes and eventually frank diabetes. Interventions which reverse this pathophysiology also benefit other risk factors of cardiovascular disease (CVD). We examined the effect of an integrative health intervention (beyond traditional approaches) on the CVD risk profile of subjects with IR characterized by elevated Homeostatic Model Assessment (HOMA). **Methods:** Consecutive subjects of the Integrative Cardiac Health Project Registry, a 12-month CVD health intervention focusing on four pillars: nutrition, exercise, stress and sleep improvement, completed validated questionnaires and laboratory tests. Subjects were categorized for IR (HOMA $\geq$ 2.8). Differences were analyzed using t-test. **Results:** Of 630 subjects, 70 had diabetes and were excluded from analysis, 207 subjects (33%) had IR by HOMA (63% women, mean age 55 ± 12 years, 56% White, 36% Black, 4% Hispanic). Of 207 IR subjects, 70 (34%) reverted to normal HOMA values upon completion of the intervention.

Risk Factor (n=207)	Baseline	12-month	p value
Fasting Glucose (mg/dL)	99.3 ± 11.5	96.4 ± 11.5	0.009
Fasting Insulin (uIU/mL)	19.4 ± 7.9	16.4 ± 9.3	0.0001
HOMA [(Glucose x Insulin)/405]	4.78 ± 2.21	3.96 ± 2.40	0.0001
Total Cholesterol (mg/dL)	181.1 ± 41.0	172.6 ± 38.1	0.03
Low Density Lipoprotein (mg/dL)	109.9 ± 35.0	103.2 ± 33.9	0.004
Triglyceride (mg/dL)	139 ± 109	117 ± 63	0.03
Body Mass Index (kg/m^2)	32.4 ± 4.8	31.6 ± 4.9	0.08
Rate Your Plate (78 points)	60.4 ± 7.4	66.1 ± 6.2	0.0001
Aerobic Exercise Time (min/week)	124 $\pm$ 127	191 $\pm$ 120	0.001
Perceived Stress Scale (56 points)	21.2 ± 8.7	17.6 ± 8.2	0.0001
Pittsburg Sleep Quality Index (21 points)	7.3 ± 4.0	5.7 ± 3.8	0.0001
Fatigue Score (10 points)	4.5 ± 2.3	3.4 ± 2.3	0.0001

Conclusions: As characterized by this population, a comprehensive approach to CVD risk reduction is warranted given the elevated risk facing menopausal women. An integrative health intervention, beyond traditional measures, emphasizing combined improvements in nutrition, exercise, stress and sleep can arrest the pathophysiology of IR, preventing development of diabetes.

6. Kashani M, Eliasson A, Walizer E, Fuller C, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Reversing prediabetes when diet and exercise are not enough. (Accepted to PCNA 2017 Annual Symposium)

Background: Diet and exercise are primary interventions for the management of cardiovascular disease (CVD). Despite healthy dietary patterns and substantial amounts of exercise in our

patient population, prediabetes persists. We sought to determine if factors other than diet and exercise are associated with prediabetes reversal. **Hypothesis:** We hypothesized that non-traditional lifestyle factors play a role in the reversal of prediabetes. **Methods:** Participants in our Integrative Cardiac Health Project Registry underwent comprehensive evaluation for CVD risk by a nurse practitioner including cardiac-relevant laboratory tests and validated questionnaires for diet (Rate-Your-Plate, RYP), exercise (minutes/week), perceived stress (Perceived Stress Scale, PSS), and sleep (Pittsburgh Sleep Quality Index). Patients with prediabetes, defined by fasting glucose 100 to 139 mg/dL, were assessed after a 12-month healthy lifestyle coaching intervention. Differences were assessed using paired t-tests. **Results:** Of 146 participants with prediabetes, 76 (52%) reversed prediabetes by fasting glucose. These reversers (mean age 64.2±13.0 years, 60% women, 64% White, 24% Black, 12% other) averaged healthy diet scores at baseline and exercised more than 150 minutes per/week as currently recommended in guidelines. Stress and sleep scores improved substantially in response to the intervention. Significant improvements were seen in reversal of insulin resistance as demonstrated by HOMA<2.8.

	Diet (RYP) of 78 points	Exercise min/week	Perceived Stress of 56 points	Sleep Quality of 21 points	Glucose mg/dL	Insulin mU/L	HOMA [Glu*ins]/405
Baseline	62.6±7.7	169±133	21.0±8.4	6.8±3.4	105.0±5.4	13.2±9.1	3.4±2.4
12 Months	67.2±5.2	205±103	17.3±6.8	5.5±3.7	93.1±4.8	9.6±6.6	2.2±1.5
p value	<0.0001	0.07	<0.0001	0.002	<0.0001	<0.0001	<0.0001

Conclusions: Given that lifestyle behavior modification is the cornerstone of prediabetes reversal, the addition of stress and sleep management to a regimen of diet and exercise is both valuable and critical to ensure a comprehensive approach to achieve normal glucose metabolism and prevent the onset of diabetes.

7. Kashani M, Eliasson A, Fuller C, Walizer E, Turner E, Tschiltz N, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. A single measurable outcome tool for tracking behavioral change. (Accepted to AHA QCOR 2017 Scientific Session)

Background: Although healthy lifestyle behaviors have been shown to significantly reduce cardiovascular disease (CVD), offsetting even genetic risk, most CVD programs focus solely on risk scores rather than calculating health improvement. We sought to validate a newly developed quantitative composite healthy lifestyle behavioral score, the Optimal Health Impact Factor (OHIF), which captures behavioral change by attainment of thresholds established by clinical guidelines. **Methods:** Patients in the Integrative Cardiac Health Project's 12-month Registry, a prospective lifestyle change program for the prevention of CVD, underwent traditional risk assessment by a nurse practitioner. Additionally, at baseline and 12-months, OHIF scores were calculated using validated questionnaires in the following four domains: nutrition (Rate-Your-Plate), exercise (minutes of continuous exercise per week), stress (Perceived Stress Scale) and

sleep (Pittsburgh Sleep Quality Index). Each domain has a gradient of three behavioral threshold scores (not at goal, red=1; almost to goal, amber=2; at goal, green=3) for a maximum of 12 possible OHIF points representing optimal health behaviors. All patients received motivational health coaching by a multidisciplinary team. Data were analyzed by t-tests, comparing measures at baseline and at 12-months. **Results:** Of 225 consecutive completers (48% men, age 56.8 ± 12.9 years, 145 White, 54 Black, 26 other, 61% at high risk by family history of CVD in first order relatives), 160 (71%) showed clinically and statistically significant improvements in the four behavioral domains and selected laboratory data.

	Change in OHIF Score by Behavioral Domain					**Lab Data**	
n = 225	**Diet (of 3 pts)**	**Exercise (of 3 pts)**	**Stress (of 3 pts)**	**Sleep (of 3 pts)**	**OHIF Score (of 12 pts)**	**T Chol (mg/dl)**	**LDL Chol (mg/dl)**
Baseline	2.54 ± 0.52	2.12 ± 0.83	2.41 ± 0.83	2.26 ± 0.52	9.32 ± 1.56	187.7 ± 40.9	114.1 ± 35.5
12-Month	2.88 ± 0.33	2.56 ± 0.64	2.61 ± 0.74	2.56 ± 0.51	10.61 ± 1.39	176.4 ± 39.4	105.2 ± 34.2
p value	<0.0001	<0.0001	0.007	<0.0001	<0.0001	0.003	0.007

Conclusions: Improvements in healthy lifestyle behaviors captured by the OHIF score correlate significantly with improvements in critical CVD risk factors, even in a population with high genetic risk. The OHIF score emphasizes gradients of positive lifestyle behavior change for both patient and provider to facilitate development of an actionable behavioral health plan to reduce CVD. Clinicians who calculate a CVD risk score may also find clinical value in calculating a composite OHIF score as a single measurable outcome tool for tracking behavioral changes longitudinally.

8. Eliasson A, Kashani M, Fuller C, Walizer E, Turner E, Tschiltz N, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. A novel lifestyle change program identifies and improves cardiovascular risks in middle-aged women. (Accepted to American Thoracic Society 2017 Meeting)

Rationale: Cardiovascular disease (CVD) is the leading cause of death in women over age 25, killing nearly twice as many women in the United States as all types of cancer combined. Women with CVD often present with atypical symptoms and identification of risk with traditional risk assessment tools remains unrecognized. We sought to identify CVD risk for women attending our cardiovascular health program (CHP) and to utilize a comprehensive intervention to improve relevant behaviors in this vulnerable, potentially overlooked population. **Methods:** Consecutive subjects entering the CHP completed validated behavioral surveys in four domains of cardiovascular health: diet, exercise, perceived stress and sleep. The surveys included Rate-Your-Plate for diet, queries for exercise minutes per week in periods of at least 10 minutes, Perceived Stress Scale, and total sleep time. Surveys were completed before and after a 12-

month multifaceted lifestyle change program. Upon entry, subjects were assessed for maladaptive behaviors for CVD and a FRS was calculated by a nurse practitioner. Subjects then received personalized motivational health coaching from an interdisciplinary team. Behavioral changes were evaluated using paired t-tests. **Results:** Of 248 consecutive program completers, 128 (52%) were women, mean age 56.2 ± 13.0 with racial diversity (76 White, 37 Black, 3 Hispanic, 3 Asian, 9 other). Upon entry to the CHP, numerous risk factors for CVD were confirmed in these women including high proportions of family history of premature CVD (44%), menopause (52%), diagnosis of depression (31%), high likelihood for obstructive sleep apnea (50%), abnormal carotid intimal media thickness (58%), obesity (mean body mass index 30.2 kg/m^2), insulin resistance (mean Homeostatic Model Assessment 2.92), prediabetes (mean HgA1C 5.74%), and CRP (mean 0.355 mg/dL). Only 3 of 128 (2%) were smokers and all 3 quit. Despite extensive indicators of high risk, mean Framingham Risk Score of 4.9 indicated low risk for CVD. After 12 months of motivational health coaching from the interdisciplinary team, clinically relevant improvements were demonstrated in each behavioral category.

n=128	Rate-Your-Plate (26-78 points)	Exercise (min/week)	Perceived Stress Scale (0-56 points)	Total Sleep Time (hrs/ 24 hrs)
Baseline	62 ± 7	143 ± 139	21 ± 9	6.5 ± 1.3
12-months	68 ± 5	219 ± 187	17 ± 8	6.9 ± 1.2
t test	<0.0001	0.0003	0.0004	0.01

Conclusion: Middle-aged, perimenopausal women are at a substantially increased risk for CVD, risk that may go undetected with conventional assessment. Our CHP targets this population by using a comprehensive approach to identify cardiometabolic risks combined with validated questionnaires to quantify maladaptive lifestyle behaviors. Improving maladaptive behaviors with a novel and personalized health program reduces overall CVD risk and ultimately lowers the leading cause of death among women.

9. Eliasson A, Kashani M, Fuller C, Walizer E, Engler R, Villines T, Vernalis M. Prevalence of sleep disturbances and their consequences in patients at risk for cardiovascular disease. (Submitted to APSS 2017 Scientific Session)

Introduction: Disturbed sleep is strongly associated with incident cardiovascular disease (CVD). We report the prevalence of sleep disturbances and their sequellae in patients attending our CVD prevention program, a population at increased risk of CVD. **Methods:** At program entry, patients completed validated questionnaires: Berlin Questionnaire for sleep apnea, Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Stanford Fatigue Scale. Means and standard deviations provide descriptive statistics and Pearson correlations describe pertinent associations. **Results:** Of 485 consecutive program participants (mean age 60.5±13.6 years, 70% women, 65% White, 27% Black, 4% Hispanic, 5% other) only 11% were diagnosed with coronary disease and 2% with stroke. Screening for sleep apnea was positive in

49% of participants and sleep apnea was previously diagnosed in 26%. Mean PSQI was 7.1±3.9, with 39% normal sleepers (PSQI<5), 43% with mild derangement, 13% moderate, and 5% severe. Mean total sleep time (TST) was 6.3±1.3 hours with only 41% getting the recommended 7 or more hours per night. Of the other participants, 30% slept 6 to 7 hours, and 28% slept less than 6 hours. Mean sleep latency was prolonged at 19.0±26.7. Mean ESS was 8.7±5.5 but 40% scored in the sleepy range (ESS≥10 of 24). Mean fatigue score was 4.3±2.4 with 47% scoring in the fatigued range (score≥5 of 10). Increased levels of perceived stress were strongly correlated with poor sleep quality (*Pr*=0.452) and increased fatigue scores (*Pr*=0.430), and mildly correlated with daytime sleepiness (*Pr*=0.267). **Conclusions:** Participants in our CVD prevention program, a population at increased risk for CVD, show evidence of substantial sleep disturbances. Nearly 3/4 of our population screens positive for sleep apnea and a majority experiences poor sleep quality and low TST. Poor sleep quality and consequent daytime symptoms correlate with increased levels of perceived stress, magnifying CVD risk.

10. Tschiltz N, Eliasson A, Halsey J, Walizer E, Kashani M, Villines T, Vernalis M. Dietitians in the kitchen impact cardiovascular disease prevention. (Submitted to Society for Nutrition Education and Behavior 2017)

Objective: To describe a successful dietetics intervention in an integrative cardiovascular health program. **Target Audience:** Dietitians caring for patients at risk for cardiovascular disease (CVD). **Theory, Prior Research, Rationale:** Amid the CVD epidemic, opportunities to learn basic cooking skills are decreasing while rates of eating out are continually increasing. Our research kitchen offers a unique opportunity to teach simple, Mediterranean-style, heart-healthy cooking techniques for use at home. **Description:** The Integrative Cardiovascular Health Program (ICHP) follows evidence-based guidelines to measure CVD risk and contributory lifestyle behaviors. Subsequent interventions include a workshop, behavioral prescriptions, and coaching follow-up over 6 months, including appointments with a dietitian for diabetes education. The four-hour interactive workshop presents overviews on diet, exercise, stress management, and sleep. The program's capstone is a food preparation demonstration and Mediterranean-style meal in the research kitchen by a Culinary Institute of America-trained chef/Registered Dietitian. The goal is to teach simple recipes that taste good and empower attendees to plan, shop and prepare healthy meals at home. **Evaluation:** After workshop participation, patients (n=603, mean age 57±12 years, 44% men) expressed strong likelihood to try Mediterranean-style recipes (mean 3.8 of 4 points). Satisfaction was 99% with the Mediterranean-style meal. Confidence was strong in 95% of patients regarding where to shop for food. At program completion, 88 of 161 patients with prediabetes (55%) normalized fasting glucose. Of 221 patients with hypercholesterolemia, 96 (43%) normalized total cholesterol. Overweight patients (n=491, 81%) averaged 2.1 kg weight loss. **Conclusions and Implications:** Interactive experiences in a research kitchen with dietitians teaching recipe planning, shopping, and meal preparation, enhance cardiovascular health outcomes.

Discussion of Stated Goals not Met:

The ICHP Risk Assessment Model is Nurse Practitioner (NP) based and subsequent delays in NP hiring/onboarding contributed significantly to recruitment/enrollment goals not being met in the past year as well as a critical element in continued data collection. In September/October 2016, ICHP made hiring offers to 1 full-time NP and 2 part-time NPs. Hiring was contingent on outcomes of both security checks and WRNMMC privileging. As of this report, 1 part-time NP

has onboarded and is currently in the clinical training phase under the direction of the Associate Medical Director. The full-time NP has an interim clearance and WRNMMC privileges have been approved; onboarding is expected early April 2017. The hiring process which includes an interim security check and WRNMMC privileging has taken 6 months for these NPs. The second part-time NP has an interim security clearance, but WRNMMC privileges are pending. To keep a patient flow for the program, Dr. Kashani has seen new and outcome participants as her schedule permits.

Study 2: Assessing Risk Factors for Cardiovascular Disease in Individuals with Major Injury (With or Without Amputation) versus No Injury

Dr. Alison Pruziner, WRNMMC Department of Rehabilitation, is the PI for this study and is responsible for recruitment/enrollment goals of this protocol. During this period of performance, 13 new subjects have been enrolled; total enrollment = 67. ICHP has continued to support CV specific data collection for these subjects, although, collection of carotid ultrasound is no longer being performed by ICHP. Given low enrollment, no interim data analysis has been performed. PI is continuing the search for funding to hire a research assistant or other recruitment support to enhance overall study enrollment. Protocol was reviewed by Scientific Advisory Board and approved. Legacy protocol transferred to eIRB system on 28 Sep 16; approval received 22 Nov 16. Annual Continuing Review submitted to WRNMMC IRB via eIRB system on 15 Dec 16; approved 30 Jan 17; acknowledged by MRMC HRPO on 17 Feb 17.

Study 3: CHP Cognitive-Behavior Therapy for Insomnia (CHP CBT-I) Study

The following major activities have been accomplished in the past year:

1) Reviewed by Scientific Advisory Board and approved
2) 2 subjects enrolled and consented for Phase 1; Total enrollment = 5.
3) Phase 1 data collection on 4 participants (2 treatment; 2 controls) complete.
4) Processes for scheduling of these study participants and data collection in place.
5) MAJ Ware reassigned out of area to complete doctoral program requirements and LTJG Lee (USUHS student) added to protocol as Associate Investigator to replace MAJ Ware in delivering CBT intervention when recruitment resumed; however, no new enrollment since 1st quarter due to ICHP-CHP enrollment issues as discussed above.
6) LTJG Lee will be completing her USUHS work this summer; 2 new USUHS students identified for delivery of CBT intervention once enrollment resumes. These 2 students will be added to protocol as AIs in the next quarter.
7) ICHP has kept communication lines open with MAJ Ware, LTJG Lee and new USUHS students during this transition process.
8) Annual Continuing Review (for expiration on 7 Jun 17) submitted to WRNMMC IRB via eIRB system on 8 Apr 17; pending approval.
9) Amendment approved by WRNMMC IRB on 23 May 16 to add LTJG Lee as an AI, inclusion of new HIPAA preparatory research provision, and edits to correct previous inconsistencies in the protocol.

Study 4: UPLIFT (Ultra-Personalized Laboratory-Risk Intervention For Treatment) for Cardiovascular Health: Cardiovascular (CV) Disease (CVD) Risk Study

The following major activities have been accomplished in the past year:

1) Reviewed by Scientific Advisory Board and approved
2) Decision made by program to submit UPLIFT Part 1 of the proposed protocol (analysis of existing bio samples) as an amendment to an existing WRNMMC IRB approved protocol; protocol currently through Immunization Healthcare Branch (IHB). UPLIFT Part 2 would be submitted through WRNMMC IRB as a new protocol. This would allow a portion of the new proposed science to be executed in a timelier manner while submission/approval of Part 2 (a more complex design) takes place.
3) Part 1 submission – amendment to approved IHB protocol (90% complete)
4) Part 2 submission - protocol development (40% complete):
5) Coordinate with Fort Detrick [Systems Biology Enterprise (SBE), Integrative Medicine Division site for data sharing agreements and CRADA between SBE, USAMRMC, HJF and WRNMMC (80% complete)
6) Joint agreements between ABBOTT LABS, HJF, MRMC, WRNMMC (70% complete)
7) Joint agreements between LabCorp (Liposciences Division), HJF, MRMC, WRNMMC (70% complete)
8) Coordinate with Army Analytic Unit for MHS database surveillance strategies and costs, letter of support (50% complete)
9) Establish Data Dictionary and Data Management Plan (85% complete)
10) Complete and review data dictionary elements for data repository and analysis planning (75% complete)
11) Develop cost-effective database management for new protocol (e.g., modify existing databases for use in current protocol and/or develop new collaborations to support complex data management/analyses-e.g. SysBioCube Program-see also https://sysbiocube-abcc.ncifcrf.gov/) (35% complete)
12) Coordinate with Fort Belvoir site for material transfer agreements (MTAs) and data sharing/clinical trial agreements (CTAs) submission (5% complete) ON HOLD

What opportunities for training and professional development has the project provided?

During this period of performance, the project has provided clinical staff with numerous opportunities for professional development in their respective fields of expertise. Opportunities existed not only to disseminate the project's research findings, but also to expand individual knowledge relating to current trends and findings in the scientific community. A listing of the conferences and training opportunities attended by ICHP clinical staff is outlined below.

- The Medical Director, Associate Medical Director and Senior Physicians Consultants attended specialty conferences not only to present ICHP scientific findings, but to attend scientific sessions in their respective areas of expertise:
    - 66th Annual Scientific Session of the American College of Cardiology (ACC 2017) Scientific Session
    - Military Health System Research (MHSRS) Symposium 2016
    - Associated Professional Sleep Societies 2016

- The two ICHP Dietitians and the Stress Reduction Specialist completed the online "AM I HUNGRY?" Mindful Eating for Diabetes, Facilitator Training course. This course met the 30 hours of continuing education required for their respective "Wellcoaches" Health Coach recertification.
- All ICHP clinical staff attended the Society of Behavior Medicine (SBM) 37th Annual Meeting & Scientific Session in Washington, DC.

How were the results disseminated to communities of interest?

ICHP has disseminated findings to communities of interest in the following manner:
1) Publications to the American Heart Association, American College of Cardiology and the Preventive Cardiovascular Nurses Association as referenced throughout this report.
2) Presentation to the WRNMMC Cardiology staff as part of their Graduate Medical Education program on "Inflammation and Cardiovascular Disease".
3) Briefing to the Joint Staff as part of the Competency Based Assessment document preparation.

What do you plan to do during the next reporting period to accomplish the goals?

Once our new NP hires are fully trained and practicing independently, we plan to continue with our publication plan as well as external outreach. We will increase recruitment efforts through a variety of ways, including base wide distribution of ICHP marketing materials, website development, departmental visits/outreach to outlying clinics, and re-establishing contact with previous referral sources.

We also plan to submit Study #4, UPLIFT (Part 1) next quarter and UPLIFT (Part 2) by June 2017 to WRNMMC Department of Research Programs.

An interim data analysis for Study #2 of the lifestyle surveys collected in those enrolled participants is planned.

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

The ICHP manuscript below was cited as evidence for the following national clinical guideline: 2016 AHA/ACC Clinical Performance and Quality Measures for Prevention of Sudden Cardiac Death. The new guidelines states collecting family history of sudden cardiac death in general practice provides opportunities to personalize risk factor counseling and modification.

Manuscript citation: Kashani M, Eliasson A, Vernalis M, Costa L, Terhaar M. Improving assessment of cardiovascular disease risk by using family history: An integrative literature review. *J Cardiovasc Nurs* 2013 Nov-Dec;28(6):E18-E27.

Guideline Citation: Al-Khatib SM, Yancy CW, Solis P, et al. 2016 AHA/ACC Clinical Performance and Quality Measures for Prevention of Sudden Cardiac Death: A Report of the

American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol* 2016;Dec 19:[Epub ahead of print].

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

ICHP has developed a lifestyle management model for optimal cardiovascular and overall health that is specific for the military as well as applicable to the general population. Through the continued work at ICHP, precision strategies have been identified for the early detection, monitoring and reduction of preclinical disease.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

There have been no changes to the methodology or approach of our studies. However, as mentioned earlier, ICHP has chosen to alter the submission process of the proposed new science (Study #4, UPLIFT) as the following for expediency:

-Part 1, analysis of existing samples from the Immunization Healthcare Branch (IHB) repository, as a modification to an already approved WRNMMC IRB protocol.

-Part 2, prospective cohort study, as a new protocol through WRNMMC Department of Research Programs.

Actual or anticipated problems or delays and actions or plans to resolve them

Study #1:

ICHP continues to be without a full-time nurse practitioner (NP) for the Cardiovascular Health Program since July 2015. A part-time NP was onboarded in Feb 2017 after a 5-month wait for an interim security clearance and WRNMMC privileging. A second part-time NP is still awaiting approval of WRNMMC privileges, but has chosen not to onboard until September 2017 due to family reasons. As previously stated, the inability to quickly onboard along with a cadre of trained NPs has severely impacted the ability to recruit new patients for the data registry. Therefore, enrollment goals have not been met in the first year. Dr. Kashani, Associate Medical

Director is seeing new and outcome participants as her schedule permits in an effort to produce a small stream of patients in the program so that the ICHP clinical team can maintain their own clinical skills and integrity of the ICHP Model. The ICHP Risk Assessment Model is Nurse Practitioner based and this delay in hiring/onboarding continues to be an **extremely critical element in recruitment, enrollment and data collection.** The problem of long hiring delays is compounded by the fact that good potential employees look for new employment opportunities and the hiring process must begin again, further delaying ICHP clinical/research work. Additionally, we have experienced a reduction in staff morale as staff want to be actively engaged in their clinical duties. ICHP will also need to remarket the program as there has been a decline in referrals due to our very long waitlist and having to prioritize enrollment when new patients can be seen.

With a trained team of NPs and a seasoned clinical staff, ICHP can now increase recruitment efforts to enroll new patients. Once the new NPs are completely trained, a full appointment schedule can be opened with the intent of eliminating our wait list as well. ICHP will be participating in several activities within the next quarter to provide a new found visibility of the program to healthcare providers and beneficiaries.

We have redesigned processes to reduce the backlog of established patients and move them to completion of at least the 6-month onsite program. The more efficient, streamlined process we established last quarter to reduce outcome visit appointment time with the NP is working well. This process allows the patient to be seen for data collection in a shorter visit, yet still have the very important dialogue for CV risk management with the NP via a telephonic consult.

Conclusions of data analysis for the carotid intima medial thickness (CIMT) measurements collected as part of the CHP were equivocal at best and did not provide predictive value for ICHP outcome analysis. In light of these conclusions, ICHP made a decision to stop CIMT collection and subsequently elimination of the sonographer position. Consideration is being given to change modalities (i.e. EBCT) for intermediate/ high risk patients in lieu of CIMT for risk stratification purposes. This can be done on a referral basis. **Therefore, Study #1, Major Task #4 will not be accomplished and not accomplishing this task will not change the methodology of this study.**

Study #2:
ICHP will continue to support data collection of EKG and ICHP questionnaires for risk assessment as recruitment continues. PI is aware that ICHP is no longer collecting CIMT data and there are no plans to continuing collection of CIMT as part of this study or amended this study with a surrogate measure.

Study #3:
ICHP will remain in contact with MAJ Ware and LTJG Lee (USUHS) as we move forward with plans to begin enrollment. We have identified two new USUHS students to replace LTJG Lee and will begin to train them on study processes/procedures once we have an approved protocol modification added them as AIs. The new USUHS students have already received CBT-I training and are not planning to be relocated in the near future.

Study #4:
CRADA(s) and other joint agreements are being reviewed by multiple parties (HJF, MRMC and WRNMMC) and are slowly progressing. We anticipate completion of the SBE CRADA by next quarter. Due to the complexity of coordination for this study and schedule challenges with collaborators, we continued to experience some stressors on our timeline to achieve final submission and reviews. As discussed earlier, ICHP has elected to submit UPLIFT Part 1 (analysis of existing bio samples) as a modification to a WRNMMC IRB approved protocol through the Immunization Healthcare Branch. It was anticipated that submission of UPLIFT Part 1 and Part 2 as a new protocol could be a lengthy approval process and severely disrupt our study timelines. Submission of Part 1 as a modification would be a more expeditious manner and allow ICHP to begin our scientific work for the UPLIFT protocol. We plan protocol submission for IRB review in February 2017.

Changes that had a significant impact on expenditures

ICHP has experienced a low burn rate during this period of performance due to various factors. One factor has been the delay in charging personnel costs on the current award due to transitioning protocols from the old award to the new award and phasing out activities attributed to the old award, causing a two month initial delay. In addition, extreme delays in hiring/onboarding Nurse Practitioners (critical ICHP personnel) due to security clearance and credentialing requirements, along with the ensued loss of candidates due to onboarding delays critically affecting Study #1 and #3 recruitment. Study #1 has enrolled 13% of its target enrollment of 35/quarter, cumulative to date 140 patients. The last factor is due to vacation time taken and other efforts such as solicitation for additional funds not charged to ICHP; however, not causing an adverse impact to the program. ICHP will move the timelines for the milestones affected by the above mentioned issues to the out years 2 and 3.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects.

NA

Significant changes in use or care of vertebrate animals.

NA

Significant changes in use of biohazards and/or select agents

NA

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**

Journal publications.

Sandrick J, Tracy D, Eliasson A, Roth A, Bartel J, Simko M, Bowman T, Harouse-Bell K, Kashani M, Vernalis M. Effect of a counseling session bolstered by text-messaging on self-selected health behaviors in college students--A preliminary randomized controlled trial. Accepted for publication in *JMIR Mhealth Uhealth*, Feb 2017. *(Acknowledgement of federal support – YES)*

Ellsworth DL, Costantino NS, Blackburn HL, Engler, RJM, Kashani M, Vernalis MN. Lifestyle modification interventions differing in intensity and dietary stringency improve insulin resistance through changes in lipoprotein profiles. *Obes Sci Pra* 2016 Sep;2(3):282-292. DOI: 10.1002/osp4.54. Epub 25 JUL 2016. *(Acknowledgement of federal support – YES)*

Books or other non-periodical, one-time publications.

Ellsworth DL, Costantino NS, Blackburn HL, Engler RJM, Vernalis MN. Cardiac interventions differing in lifestyle modification improve insulin resistance through changes in lipoprotein profiles. *Circulation* 2016;133:AP108. *(Acknowledgement of federal support – NO)*

Kashani M, Eliasson A, Fuller C, Walizer E, Engler R, Villines T, Vernalis M. Strategies to boost self-efficacy promote multicomponent behavior changes. *Ann Behav Med* 2016; 50 Suppl 1:S124. doi:10.1007/s12160-015-9766-4 *(Acknowledgement of federal support – NO)*

Eliasson A, Kashani M, Fuller C, Walizer E, Engler R, Villines T, Vernalis M. Targeted behavioral interventions improve disturbed sleep. *Sleep* 2016; 39:A397 *(Acknowledgement of federal support – NO)*

Engler R, Kashani M, Eliasson A, Walizer E, Fuller C, Villines T, Vernalis M. Blood pressure elevations below hypertension threshold linked to insulin resistance and dyslipidemia: an under-recognized cardiovascular disease risk phenotype. Military Health System Research (MHSRS) Symposium 2016. Published in Conference Proceedings. *(Acknowledgement of federal support – YES)*

Kashani M, Eliasson A, Fuller C, Walizer E, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Arresting insulin resistance with an integrative health intervention. *J Am Coll Cardiol*. 2017; 69(11S):1853. doi.org/10.1016/S0735-1097(17)35242-7 *(Acknowledgement of federal support – NO)*

Kashani M, Eliasson A, Walizer E, Fuller C, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Multidisciplinary cardiovascular team review captures preclinical disease. *J Am Coll Cardiol*. 2017; 69(11S):2103. doi.org/10.1016/S0735-1097(17)35492-X *(Acknowledgement of federal support – NO)*

Kashani M, Eliasson A, Walizer E, Fuller C, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Reversing prediabetes when diet and exercise are not enough. (Accepted to Preventive Cardiovascular Nurses Association (PCNA) 23rd Annual Symposium). *(Acknowledgement of federal support – NO)*

Eliasson A, Kashani M, Fuller C, Walizer E, Turner E, Tschiltz N, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. A novel lifestyle change program identifies and improves cardiovascular risks in middle-aged women. (Accepted to American Thoracic Society 2017 Meeting, May 2017) *(Acknowledgement of federal support – NO)*

Eliasson A, Kashani M, Fuller C, Walizer E, Engler R, Villines T, Vernalis M. Prevalence of sleep disturbances and their consequences in patients at risk for cardiovascular disease. (Accepted to APSS 2017 Scientific Session, June 2017) *(Acknowledgement of federal support – NO)*

Tschiltz N, Eliasson A, Halsey J, Walizer E, Kashani M, Villines T, Vernalis M. Dietitians in the kitchen impact cardiovascular disease prevention. (Submitted to Society for Nutrition Education and Behavior 2017, July 2017) *(Acknowledgement of federal support – NO)*

Kashani M, Eliasson A, Walizer E, Fuller C, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Reversing prediabetes when diet and exercise are not enough. Walter Reed National Military Medical Center, Department of Research Program, 2017 Research and Innovation Month, Bethesda, MD, 1-5 May 2017 (Submitted for Robert A. Phillips Research Award competition poster) *(Acknowledgement of federal support – NO)*

Tschiltz N, Eliasson A, Halsey J, Walizer E, Kashani M, Villines T, Vernalis M. Dietitians in the kitchen impact cardiovascular disease prevention. Walter Reed National Military Medical Center, Department of Research Program, 2017 Research and Innovation Month, Bethesda, MD, 1-5 May 2017 (Submitted for Paul Florentine Patient and Family-Centered Care competition poster) *(Acknowledgement of federal support – NO)*

Other publications, conference papers, and presentations.

Eliasson A, Kashani M, Fuller C, Walizer E, Engler R, Villines T, Vernalis M. Targeted behavioral interventions improve disturbed sleep. APSS, Denver, CO, 11-15 June 2016 (poster)

Engler R, Kashani M, Eliasson A, Walizer E, Fuller C, Villines T, Vernalis M. Blood pressure elevations below hypertension threshold linked to insulin resistance and dyslipidemia: an under-recognized cardiovascular disease risk phenotype. Military Health System Research (MHSRS) Symposium 2016, Kissimmee, FL, 15-18 August 2016 (poster)

Kashani M, Eliasson A, Walizer E, Fuller C, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Multidisciplinary cardiovascular team review captures preclinical disease. 66th Annual Scientific Session of the American College of Cardiology (ACC 2017) Scientific Session, Washington, DC, 17-19 March 2017 (poster)

Kashani M, Eliasson A, Fuller C, Walizer E, Tschiltz N, Turner E, Grunewald M, Halsey J, Engler R, Villines T, Vernalis M. Arresting insulin resistance with an integrative health

intervention. 66th Annual Scientific Session of the American College of Cardiology (ACC 2017) Scientific Session, Washington, DC, 17-19 March 2017 (poster)

- **Website(s) or other Internet site(s)** NA

- **Technologies or techniques** NA

- **Inventions, patent applications, and/or licenses NA**

- **Other Products**

Data dictionary developed for clinical research management in order to identify CVD risk variables for statistical analysis and future data modeling.

Research Information Management System:

1) Functionality updated to match CHP appointment flow and allow for email capability/data collection at final appointment.
2) Functionality improved by loading provider recommendations with patient survey responses.
3) Functionality improved by creation of "Provider Risk Factor Letter" for quick reference of clinical/preclinical disease states.
4) Creation of a new tool "Status Feedback Sheets" for personalization of patient lifestyle prescriptions.

Clinical Review format revised to establish systematic, efficient and safe review of patient data for interdisciplinary team communication; updated/expanded to "tele-review" of clinical patient snapshot rather than standard paper review by multidisciplinary team.

CRM Capabilities Based Assessment (CBA) Document:

1) Dissemination of ICHP scientific findings at CBA team meeting with goal of improving CVD risk assessment and prevention strategies across the Department of Defense (DOD) (April 2016).
2) Approval of ICHP scientific findings at CBA team meeting to improve CVD risk assessment and prevention strategies in the DOD to be submitted to the Joint Staff. (12 Aug 2016)
3) Approval by Joint Staff of CBA document which will guide cardiovascular care across the DOD.

A full proposal, entitled “Cardiovascular Disease Risk Biomarkers in Women compared to Men in the Military Health System: Pentraxin 3 and Autoantibodies” was submitted on 19 October 2016 for funding consideration to the Congressionally Medical Directed Research Program. Proposal costs related to this proposal were not charged to the current ICHP award. This proposal addresses gaps in the understanding of cardiovascular disease risk in women compared to men, with a focus on enhanced precision of CVD risk assessment (using validated predictive biomarkers of CVD mortality/morbidity risk) that can lead to improved guidelines for earlier interventions (and lifestyle management) to reduce CVD risk

progression in the preclinical and clinical states. This submission is designed to cover unfunded requirements of the proposed UPLIFT protocol; however, decision made not to fund.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: *Marina Vernalis, DO*
Project Role: *Medical Director, ICHP*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *10.5*
Contribution to Project: *Dr. Vernalis has performed oversight for all aspects of the project, scientific direction, data analysis/clinical interpretation and manuscript development.*

Name: *Arn Eliasson, MD*
Project Role: *Clinical/Research Physician Consultant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *7*
Contribution to Project: *Dr. Eliasson has performed work in the area of sleep medicine and study design, data analysis/clinical interpretation and manuscript preparation.*

Name: *Renata Engler, MD*
Project Role: *Research Physician Consultant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *6*
Contribution to Project: *Dr. Engler has performed work in the area of scientific direction, study design, data analysis/clinical interpretation and manuscript preparation.*

Name: *Mariam Kashani, DNP, CRNP*
Project Role: *Associate Medical Director*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *11*
Contribution to Project: *Dr. Kashani has performed work in the area of scientific direction, participant risk assessment, and interpretation of clinical findings, dissemination of findings to providers, study design, implementation, data collection, data analysis /clinical interpretation and manuscript preparation.*

Name: *Elaine Walizer, MSN*
Project Role: *Director, Clinical Operations*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *11*
Contribution to Project: *Ms. Walizer has performed work in the area of daily on-site execution of research and clinical operations, informed consent, coordination of studies processes, personnel*

supervision, regulatory document maintenance, protocol management, technical reporting and manuscript preparation.

Name: *Audra Nixon, MPH*
Project Role: *Chief, Operations*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *2*
Contribution to Project: *Ms. Nixon has performed work in the area of on-site award administration, personnel supervision and coordination with various agencies.*

Name: *Marilyn Grunewald, MSW*
Project Role: *Stress Reduction Specialist*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *10*
Contribution to Project: *Ms. Grunewald has performed work in the area of the ICHP stress management intervention, data collection and participant engagement/personalized prescriptions.*

Name: *Joy Halsey, MS, RD, LD*
Project Role: *Dietitian*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *11*
Contribution to Project: *Ms. Halsey has performed work in the area of the ICHP nutrition intervention and pre-diabetes empowerment package, data collection and participant engagement/personalized prescriptions.*

Name: *Nancy Tschiltz, MS, RD, LD*
Project Role: *Dietitian*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *10*
Contribution to Project: *Ms. Tschiltz has performed work in the area of the ICHP nutrition intervention, data collection and participant engagement/personalized prescriptions.*

Name: *Ellen Turner, MS*
Project Role: *Health Coach, Coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *11*
Contribution to Project: *Ms. Turner has performed work in the area of the ICHP exercise intervention, data collection and participant engagement/personalized prescriptions.*

Name: *Peta-Gay Llewellyn*
Project Role: *MRI Technician II*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *6*
Contribution to Project: *Ms. Llewellyn has performed work in the area of sonography, participant metrics and preparation of ultrasound reports.*

Name: *Kenneth Williams, MS*
Project Role: *Program & Financial Manager*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *11*
Contribution to Project: *Mr. Williams has performed work in the area of budget management and other daily operational activities.*

Name: *Claire Fuller, BS*
Project Role: *Program Manager I*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *11*
Contribution to Project: *Ms. Fuller has performed work in the area of daily on-site management of office functions, facilities management, security, personnel supervision, data management, data analysis.*

Name: *Christa Caporiccio*
Project Role: *Administrative Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *11*
Contribution to Project: *Ms. Caporiccio has performed work in the area of daily office clerical functions, patient scheduling and record management.*

Name: *Carmen Ching, CRNP*
Project Role: *Research Nurse Practitioner*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *1*
Contribution to Project: *Ms. Ching is new to program (February 2017) and has primarily performed training in preparation for her role in the clinical assessment and care management for ICHP participants.*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report.

What other organizations were involved as partners?

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

Quad charts – See attachment.

9. APPENDICES: None

Integrative Cardiac Health Project (ICHP)

Log Number 15274002
W81XWH-16-2-0007

PI: Marina Vernalis, DO **Org**: ICHP/Henry M. Jackson Foundation for Advancement of Military Medicine **Award Amount:** $7,698,400.00

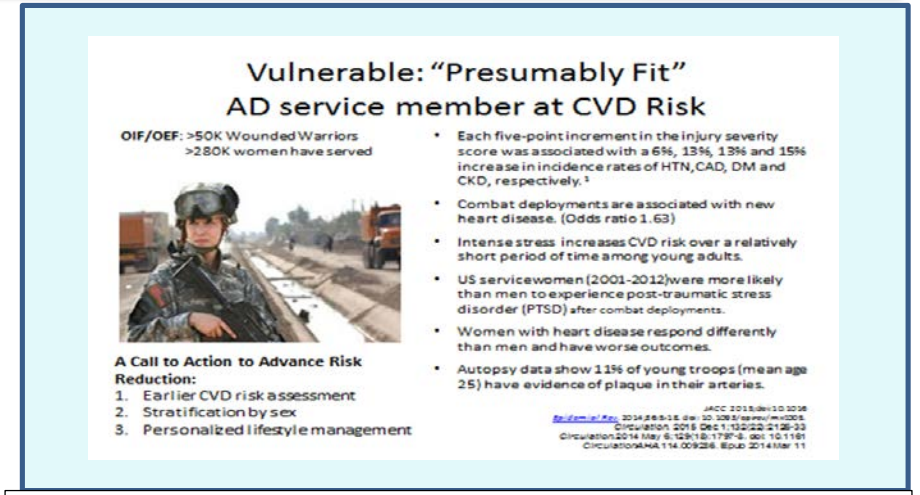
Project Aim(s)

- To evaluate and enhance Cardiovascular Disease (CVD) Risk Assessment and Risk Reduction
- To evaluate and enhance Personalized Lifestyle Management Interventions (LMI)

Approach

We will accomplished these aims through the conduct of a Cardiovascular Health Program (CHP) as well as 4 major research studies. Through prospective, longitudinal data collection and randomized controlled trial methodologies, we aim to:

1) Capture traditional and nontraditional behavioral CVD risk profiles over time; define prevalence of CVD risk in service members (SM), including those with major injury; clinical outcome surveillance
2) Target reversible CVD risks in preclinical disease stages
3) Determine impact of Cognitive Behavior Therapy for Insomnia (CBT-I) on CVD risk
4) Improve accuracy of early CVD risk assessment by gender utilizing novel biomarkers combined with traditional + behavioral CVD risk assessments
5) Team based LMI guided care using analysis of individual's comprehensive risk to target reversible risk factors in the domains of diet, exercise, sleep and stress.
6) Develop personalized LMI strategies based on more precise CVD risk assessment specific for service members with major injury
7) Improve accuracy of early CVD risk assessment by gender utilizing novel biomarkers combined with traditional + behavioral CVD risk assessment



Accomplishments: 4 abstracts presented (APSS, MHSRS, ACC); 5 abstracts accepted at international conferences; ICHP manuscript cited by 2016 ACC national guidelines on sudden cardiac death; Proposal submission for unfunded UPLIFT requirements.

Timeline and Cost

Activities CY	16-17	17-18	18-19
Study 1: CHP Registry			
Study 2: Assessing CVD Risk in SM with Major Injury			
Study 3: CBT-Insomnia Study			
Study 4: UPLIFT			
Estimated Budget ($K)	**$2.844**	**$2.850**	**$2.003**

Updated: (March 31 2017)

Goals/Milestones

CY16 Goal – Refine CVD risk assessment and reduction

CY17 Goals – Refine CVD risk assessment and reduction

☐UPLIFT protocol submission; modification to CHP to improve science
☐Complete Phase 1 CBT-I study enrollment
☐Initiate UPLIFT protocol (Part 1)
☐Begin CBT-I Phase 2 enrollment

CY18 Goal – Refine CVD risk assessment and reduction

☐Complete Phase 2 CBT-I study
☐Complete UPLIFT (Part 1)

CY19 Goal – Dissemination of research findings

☐Publish data from CBT-I study
☐Preliminary analysis of CVD risk in SM w/major trauma

Comments/Challenges/Issues/Concerns

- CY16 milestones not met due extreme personnel hiring delay & lack of statistical support for protocol development/submission; milestones moved to CY17.

Budget Expenditure to Date

Projected Expenditure: $2,844,371
Actual Expenditure: $1,809,964

ICHP Study #1 – Cardiovascular Health Program (CHP) Registry

Log Number 15274002
W81XWH-16-2-0007

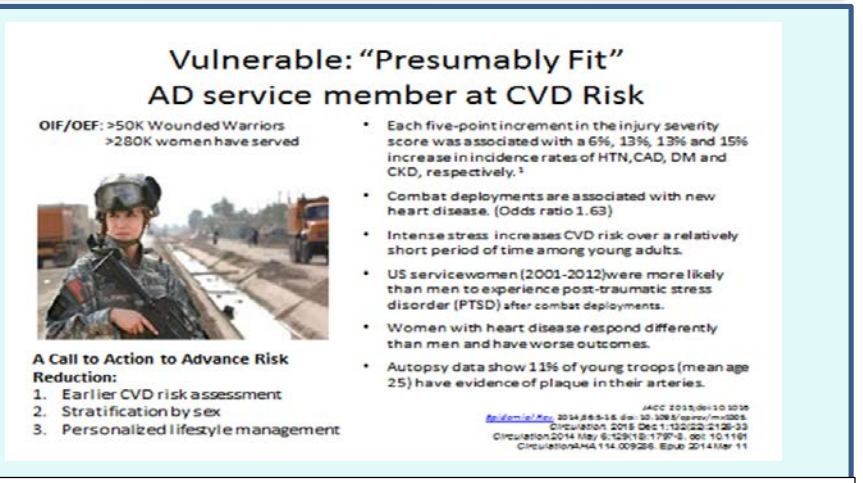
PI: Marina Vernalis, DO **Org**: ICHP/Henry M. Jackson Foundation for Advancement of Military Medicine **Award Amount:** $7,698,400.00

Study 1 Aim(s)

- To evaluate and enhance the benefits of patient-centric tools for comprehensive CVD risk assessment and reduction in the context of longitudinal outcomes.
- To evaluate and enhance the CHP lifestyle management interventions to improve patient-centric CVD risk reduction in the context of longitudinal outcomes.
- To analyze self-management behaviors (nutrition, exercise, stress and sleep) that make the military population more vulnerable to CVD due to hazardous occupational exposures.
- To improve measures of endothelial function and/or surrogate measures of atherosclerosis utilizing the ICHP CHP lifestyle management intervention in subpopulations (i.e. Caucasians vs. Non Caucasians).
- To capture patient generated data, including data (motivation, joys, barriers and self-efficacy) not routinely captured in MTF electronic health records to facilitate patient and family engagement to optimize outcomes.

Approach

All clinically derived CHP patient-related data are entered into a single, secure database to comprise the registry. Assessment of the registry database will allow queries to define the impact of an integrative lifestyle program on CVD risk over time. The registry utilizes the ICHP database which documents demographics, medical & health history, questionnaire responses, physical examination, vital signs, cardiac imaging, anthropometrics, laboratory test results, acti-graphic data, clinical recommendations, consultations, referrals, patient management, and patient visits.



Accomplishments: 1) Four abstracts presented at international conferences; 2) ICHP manuscript cited as evidence for 2016 ACC National Clinical Guideline on Sudden Cardiac Death; 3) Outcome manuscript in preparation.

Timeline and Cost

Activities CY	16-17	17-18	18-19
Study 1: CHP Registry			
Study 2: Assessing CVD Risk in SM with Major Injury			
Study 3: CBT-Insomnia Study			
Study 4: UPLIFT			
Estimated Budget ($K)	**$2.844**	**$2.850**	**$2.003**

Updated: (31 March 2017)

Goals/Milestones

CY16 Goal – Refine CVD risk assessment and reduction

CY17 Goal – Refine CVD risk assessment and reduction

All ICHP patient generated data migrated to research information system

☐ Completion of data dictionary

☐Enrollment on target

☑Development of ICHP Healthy Lifestyle Index

CY18 Goal – Refine CVD risk assessment and reduction

☐Develop new patient and provider tools for CVD risk assessment/reduction

☐New phenotype of CVD risk profile identified

CY19 Goal – Dissemination of research findings

☐Comparative analyses of CHP LMI outcomes performed

☐Manuscripts published

Comments/Challenges/Issues/Concerns

- CY16 milestones not met due to extreme delay in hiring personnel for CHP; milestones modified for CY17)

Budget Expenditure to Date

Projected Expenditure: $2,844,371

Actual Expenditure: $1,809,964

ICHP Study #2 – Assessing CVD Risk in Major Injury With or Without Amputation versus No Injury

Log Number 15274002
W81XWH-16-2-0007

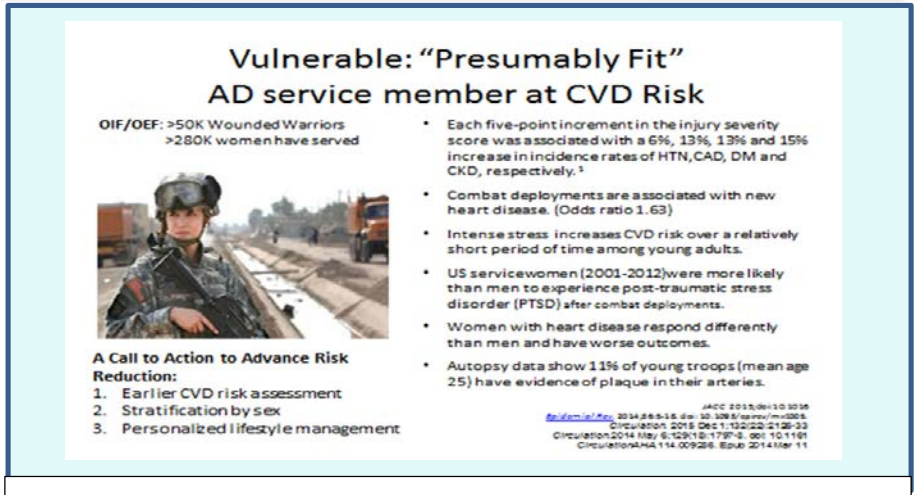
PI: Marina Vernalis, DO **Org**: ICHP/Henry M. Jackson Foundation for Advancement of Military Medicine **Award Amount:** $7,698,400.00

Study 2 Aim(s)

- To identify the specific risk factors that may contribute to an increased CVD risk in military personnel with major injury.
- To develop a comprehensive CVD risk profile in military personnel with major injury.
- To theorize the pathophysiology behind the changes in CV risk profiles in those individuals with major injury.
- To develop treatment strategies specifically targeted for a more precise CV risk stratification in populations with major injuries.

Approach

Up to 405 patients will be enrolled and divided into three groups: no injury, traumatic orthopedic injury with amputation, traumatic orthopedic without amputation. Data is collected at time of consent and at a 5-year follow-up visit. Data collection includes demographics (including diagnosis of hypertension, hyperlipidemia or diabetes mellitus), family history of CVD, anthropometrics, cardiac relevant laboratories, a Multi-Analyte Profile (~150 cardiovascular-, inflammation-, and metabolism-related biomarkers), gene expression, vital signs, electrocardiogram, cardiac imaging study, stress and sleep surveys, diet questionnaire, smoking history and activity measures. CVD risk will be estimated using the ICHP CVD risk assessment and the National Heart Lung and Blood Institute (NHLBI) 10-year risk estimate.



Accomplishments: 13 new subjects enrolled.

Timeline and Cost

Activities CY	16-17	17-18	18-19
Study 1: CHP Registry			
Study 2: Assessing CVD Risk in SM with Major Injury			
Study 3: CBT-Insomnia Study			
Study 4: UPLIFT			
Estimated Budget ($K)	**$2.844**	**$2.850**	**$2.003**

Updated: (31 March 2017)

Goals/Milestones

CY16 Goal – Continue to provide longitudinal data collection
☑All ICHP supported data collection completed
CY17 Goals – Collaborate on data analysis & interpretation of findings
☐All ICHP surveys and risk score calculations complete, validated and recorded
CY18 Goal – Assist with data analysis
☐Support and consult for data analysis
CY19 Goal – Dissemination of research findings
☐Manuscripts published

Comments/Challenges/Issues/Concerns

- PI unable to meet recruitment goals and is searching for funding to support hiring of research assistant

Budget Expenditure to Date

Projected Expenditure: $2,844,371
Actual Expenditure: $1,809,964

ICHP Study #3 – CHP Cognitive-Behavior Therapy for Insomnia (CHP CBT-I) Study

Log Number 15274002
W81XWH-16-2-0007

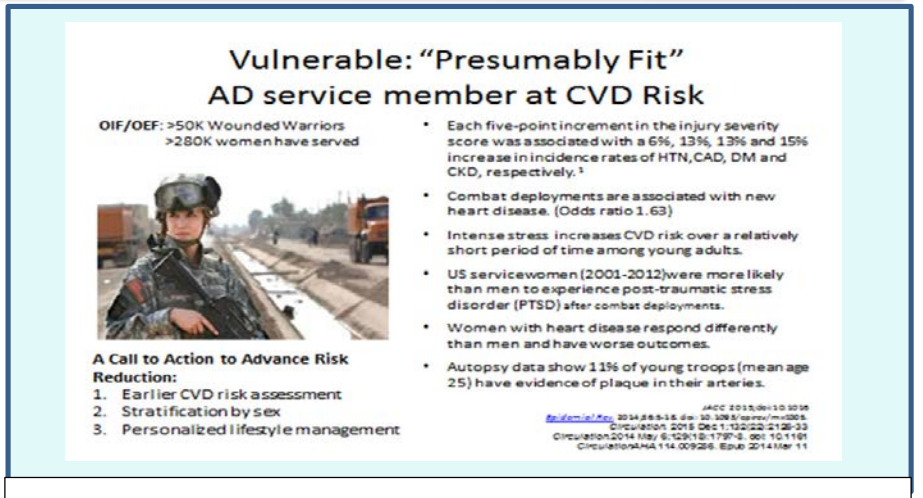
PI: Marina Vernalis, DO **Org**: ICHP/Henry M. Jackson Foundation for Advancement of Military Medicine **Award Amount:** $7,698,400.00

Study 3 Aim(s)

- To evaluate the feasibility & acceptability of CBT-I within the CHP program (Phase 1).
- To determine the variability of the effect of CHP compared to CHP + CBT-I on the primary outcome (sleep efficiency) (Phase 1).
- To determine the effectiveness of CHP compared to CHP + CBT-I on the improvement of sleep outcomes in a subset of CHP patients diagnosed with insomnia (Phase 2).
- To determine the effectiveness of CHP compared to CHP + CBT-I on symptoms of fatigue, insomnia severity, depression, perceived stress, and sleep-related quality of life (Phase 2).
- To examine data regarding the impact of the CHP program compared to CHP + CBT-I on secondary cardiovascular risk factors in a subset of CHP patients with insomnia (Phase 2).

Approach

This will be a two phase, single-center, prospective, randomized, controlled, interventional trial within ICHP: Phase I—feasibility and acceptability; Phase II—effectiveness of intervention. This study is being conducted among CHP patients who have symptoms of insomnia. Patients who meet criteria and consent to participate, are randomized to one of two conditions: (1) CHP, or (2) CHP + CBT-I treatment. CBT-I treatment will consist of four in-person appointments and two telephone appointments.



Accomplishments: None to report.

Timeline and Cost

Activities CY	16-17	17-18	18-19
Study 1: CHP Registry			
Study 2: Assessing CVD Risk in SM with Major Injury			
Study 3: CBT-Insomnia Study			
Study 4: UPLIFT			
Estimated Budget ($K)	**$2.844**	**$2.850**	**$2.003**

Updated: (31 March 2017)

Goals/Milestones

CY16 Goal – Complete Phase 1 (not met)

CY17 Goals – Complete Phase 1 and Conduct Phase 2 of protocol

☐Phase 1 data analysis and interpretation
☐Determine modification to protocol for Phase 2 implementation
☐Recruitment and enrollment completed
☐All data collected, validated and recorded

CY18 Goal – Complete Phase 2

☐Data analysis and interpretation

CY19 Goal – Dissemination of research findings

☐Manuscripts published

Comments/Challenges/Issues/Concerns

- CY16 milestone not met due to extreme delay in hiring personnel for CHP; milestones modified for CY17

Budget Expenditure to Date

Projected Expenditure: $2,844,371
Actual Expenditure: $1,809,964

ICHP Study #4 – UPLIFT (Ultra-Personalized Laboratory-Risk Intervention For Treatment) for Cardiovascular Health: Cardiovascular Disease (CVD) Risk Study

Log Number 15274002
W81XWH-16-2-0007

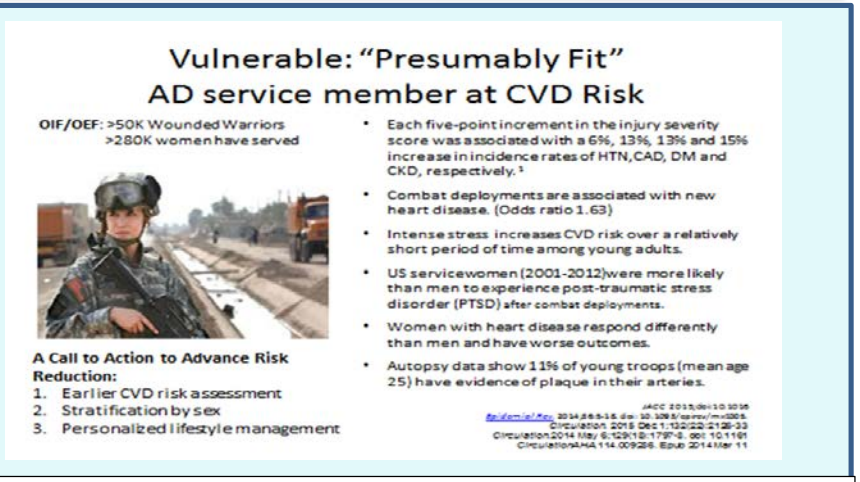
PI: Marina Vernalis, DO **Org**: ICHP/Henry M. Jackson Foundation for Advancement of Military Medicine **Award Amount:** $7,698,400.00

Study 4 Aim(s)

1: In a retrospective observational cohort design (Part 1), determine the prevalence of moderate and high risk CVD stratification (using novel predictive biomarkers)/PBMs) in a healthy pre-deployment (pre-smallpox vaccine) established cohort traditionally considered at low risk for CVD with stratification by sex.
2: In a prospective observational cohort study design (Part 2): determine the prevalence of hsTnI (coupled with us-CRP, suPAR, NT-pro-BNP, Gal-3, GlycA) risk predictive elevations [sex adjusted levels as published surrogate markers of CVD mortality/morbidity risk] in patients with or without evidence of CAD (obstructive/nonobstructive/none).

Approach

Two population cohorts, stratified by sex (one using existing biologic samples and clinical data collected between 2004-2010; a second collected prospectively), will be characterize for more precise CVD risk stratification using PBMs. Part 1 will provide the basis for evaluating the predictive CVD risk value of the PBMs using existing inpatient/outpatient diagnostic databases. Part 2 will be used to determine subclinical disease in symptomatic cardiac imaging negative patients and in those with variable degrees of coronary artery obstruction. Comprehensive data sets will be used to undertake cluster or machine learning analyses to identify subgroups/phenotypes of patients , by sex, with unique patterns of CVD risk.



Accomplishments: Significant progress had been made in refining the study design, data dictionary, data management plan and collaborations.

Timeline and Cost

Activities CY	16-17	17-18	18-19
Study 1: CHP Registry			
Study 2: Assessing CVD Risk in SM with Major Injury			
Study 3: CBT-Insomnia Study			
Study 4: UPLIFT			
Estimated Budget ($K)	**$2.844**	**$2.850**	**$2.003**

Updated: (31 March 2017)

Goals/Milestones

CY16 Goal – Submission of protocol for IRB approval (not met)
CY17 Goals –Final submission of revised protocol with Implementation
☐Completion of study modification & new protocol for submission to WRNMMC IRB
☐Finalization of data dictionary and data management plan
☐Completion of data analysis on samples (Part 1)
☐Manuscript submitted for publication
☐Implementation of Part 2 (recruitment, enrollment, data collection)
CY18 Goal – Completion of study recruitment & data collection
☐Data QC and analysis
☐Prepare and distribute outcomes surveillance plan
CY19 Goal – Dissemination of research findings
☐Manuscripts published

Comments/Challenges/Issues/Concerns

- CY16 milestones not met due to prolonged delays in statistical support & organizational procedural challenges continue to delay finalized protocol submission; milestones modified for CY17)

Budget Expenditure to Date

Projected Expenditure: $2,844,371
Actual Expenditure: $1,809,964